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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/537,338	11/21/2005	Yorihiro Yamamoto	ITO-100-PCT	3453
28892	7590	09/13/2006		
SNIDER & ASSOCIATES P. O. BOX 27613 WASHINGTON, DC 20038-7613			EXAMINER PETERSEN, CLARK D	
			ART UNIT	PAPER NUMBER

1655

DATE MAILED: 09/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

##

<b>Office Action Summary</b>	Application No. 10/537,338	Applicant(s) YAMAMOTO ET AL.	
	Examiner Clark D. Petersen	Art Unit 1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 21 November 2005.
- 2a) ☐ This action is FINAL.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-18 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-18 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

## DETAILED ACTION

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The claims are generally narrative and indefinite, failing to conform with current U.S. practice. They appear to be a literal translation into English from a foreign document and are replete with grammatical and idiomatic errors.

Claims 1-18 are also rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-18 refer to "coenzyme Q-10 and a 2-electron reduced form thereof." This phrase is vague and indefinite because "coenzyme Q-10" refers to two different molecules, ubiquinone and ubiquinol. It is assumed by examiner that applicant intends for the claims to refer to ubiquinone and ubiquinol when using the phrase "coenzyme Q-10 and a 2-electron reduced form thereof", but the claim nevertheless remains unclear.

Claims 1-18 state "the specimen....is extracted with a water-soluble organic solvent as a *pretreatment* and *extracted liquid as an analytical sample is analyzed*. It is unclear what applicant specifically means by the word "pretreatment". It is also unclear what applicant means by "extracted liquid as an analytical sample is analyzed".

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Claims 3, 4, 7, 8, 13, 14, 15, and 16 refer to storage at a *temperature within a range of a melting point of the extracted liquid and room temperature*. This phrase is vague and indefinite. A given substance has only one melting point and therefore the phrase does not define a lower (or upper?) temperature limit. Examiner assumes applicant means storage of a sample at a temperature between its freezing point and room temperature, i.e. the sample is never frozen.

Claims 5-8 and 13-16 recite a *preparatory treatment for condensing the analytical sample according to a column switching method is performed*. It is unclear what a "preparatory treatment" is. Use of the word "condensing" also renders the claims vague and indefinite, because condensing can mean either a chemical condensation or concentrating a sample by removing some portion of the solvent volume. The specification gives no guidance; examiner could only find reference to "condensing" on p. 12, lines 24-28 of the instant specification, in which applicant says "concentrating" occurs using "adsorption effect of filler, etc.". It is unclear whether this "concentrating" is synonymous with "condensing", and even if so, the specification offers no guidance as to how this step occurs. It is additionally unclear how a "column switching method" facilitates "condensing" a sample.

Claims 17-18 refer to a *liquid sending mechanism...for liquid sending*. Does applicant mean an injection system for injecting? Claims 17-18 also refer to an electrochemical detector for *detection-processing liquid*. Examiner assumes this phrase means the sample is analyzed with an electrochemical detector, but the actual meaning is unclear.

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Claims 17-18 also recite:

*A switching mechanism for switching liquid-sending routes for the mobile phases of the two series of the liquid-sending mechanism,*

*A condensation column for receiving the second mobile phase after the mobile phase of the first series is received so as to condense the analytical sample,*

*A separation column for receiving and separating liquid sent from the condensation column, and*

*A reduction column for receiving and reducing liquid sent from the separation column...*

These claims do not particularly point out and distinctly claim an invention. Does applicant intend to switch mobile phase 1 and mobile phase 2, and then recombine them in the condensation column? What is separated? Which fraction sent from the separating column is reduced? It is unclear to examiner what invention claims 17 and 18 teach.

It is also unclear from either the instant specification or the instant claims 17 and 18 how sending a first mobile phase from one sender and a sending a second mobile phase from a second sender using a column switching method contributes to measuring the amount of coenzyme Q<sub>10</sub> and a reduced form thereof. Claims 17 and 18 are so incomprehensible that a search of the art is impossible.

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Regarding claims 1-16, the instant application was compared to prior art based on assumptions examiner has made as discussed above. Prior art has been applied if it seems to teach what the instant application, however vague, seems to recite.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Edlund (J Chromatogr, 1988). Edlund teaches a method of measuring coenzyme Q<sub>10</sub> in human plasma that involves extracting coenzyme Q<sub>10</sub> with an organic solvent, namely 1-propanol, from human plasma (see *Preparation of Plasma Samples*, pp. 90-91, for example). In one embodiment this method is carried out with 2-propanol (see Table II, p. 92, for example). In particular he thaws the plasma samples, extracts the coenzyme Q<sub>10</sub> and for 45 minutes the samples remain in a liquid form before HPLC injection, meeting the limitation that the extracted samples must be stored at a temperature between their melting point and room temperature (see *Preparation of Plasma Samples*, pp. 90-91, for example). Edlund also teaches a column switching method whereby the sample can be sent through a precolumn which removes polar compounds and strongly retained solutes, removing a fraction of the sample and by definition concentrating the

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sample, meeting the limitation of condensing the sample by a column switching mechanism (see p. 90, for example). The detection system employed by Edlund comprises a coulometric system, whereby once the sample has been purified and condensed, it is oxidized, then reduced and then reoxidized to provide a uniform oxidation state to be detected by an electrochemical cell, thereby meeting the limitation that the sample is reduced and detected (see p. 90, for example). Therefore the teachings of Edlund are deemed to anticipate the instant claims 1-16.

Claims 1, 3, 5, and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Grossi, et al (J Chromatogr, 1992). Grossi et al teach methods of determining total coenzyme Q<sub>10</sub> content in human plasma samples; these methods comprise collecting both the oxidized and reduced forms of coenzyme Q<sub>10</sub>, converting the entire sample to the oxidized form, and measuring the total sample (see Introduction, particularly p. 218, column 1, for example). The coenzyme Q<sub>10</sub> is extracted from human plasma samples by combination with methanol, a water-soluble organic solvent (see Method B and Method C, p. 219, for example). Grossi et al teach that once plasma samples are thawed, and the extraction process begins, they do not freeze the extracted samples at any point, reading on the the limitation of storing the samples at a temperature between the melting point of the extracted sample and room temperature (see Methods B and C, p. 219, for example). Grossi et al also teach that they condense their samples, and that this occurs using disposable precolumns into which the samples are injected by a column switching method. According to this method, a sample is concentrated in a SPE

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cartridge and eluted with 2-propanol. This sample is then injected into a disposable precolumn, where it is washed with methanol, removing contaminants, reading on condensing the sample. Finally the sample is injected into an analytical column for separation (see pp. 219 and 220, for example). Therefore the teachings of Grossi et al are deemed to anticipate the instant claims 1, 3, 5, and 7.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Grossi et al (J Chromatogr, 1992).

Many of the teachings of the Grossi et al are discussed above and applied as before.

Grossi et al do not explicitly demonstrate the employment of 2-propanol as an agent for extracting coenzyme Q10 from plasma samples. Rather, they explicitly employ 1-propanol. However, they teach that 2-propanol and 1-propanol are equivalent in terms of being solvents for coenzyme Q-10 (see Results and Discussion, p. 220, for example).

Grossi et al also teach that column-switching methods are useful in the study of coenzyme Q10 and other components of a given liquid. They teach that "The column-

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switching technique improves the automation of the analytical procedures, greatly increasing the laboratory productivity" (see p. 218, col. 2, for example).

It would have been obvious to one of ordinary skill in the art at the time that the invention was made to employ 2-propanol as an extraction agent in a method extracting coenzyme Q10 taught by Grossi et al, because one of ordinary skill in the art knows that the solvating capacity of an extraction agent for a given compound is essential if it is be used effectively to extract that given compound, and in this case, Grossi et al teach that 2-propanol is equivalent to 1-propanol in terms of its solvating ability for Coenzyme Q10. One having ordinary skill in the art would have been motivated to make such a change as a mere alternative and functionally equivalent extraction technique and since only the expected solvating effect would have been obtained. The use of alternative and functionally equivalent techniques would have been desirable to those of ordinary skill in the art based on the *economics and availability of components*.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ a column switching method in any aspect in which one of skill in the art wishes to transfer samples from a column of one function to a column of another function, because Grossi et al teaches that the column switching technique greatly increases laboratory productivity. One would have been motivated to do so for the expected benefit of making a lab run more efficiently and collecting more data in less time.

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Based upon the teachings of the cited references, the level of skill of one of ordinary skill in the art, and absent any evidence to the contrary, one would have had a reasonable expectation of success in practicing the claimed invention.


### ***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Clark D. Petersen whose telephone number is (571)272-5358. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey can be reached on (571)272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

CDP  
8/29/2006

  
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